Case
Report**Multifocal Cholesterol Granulomas of the Thymus:
A Case Report of Positron Emission Tomography-
Positive Benign Tumor of the Anterior Mediastinum**

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Cholesterol granulomas of the thymus are extremely rare benign entities. Herein, we describe a case of cholesterol granuloma in a 45-year-old man who presented with multifocal anterior mediastinal lesions on computed tomography (CT). Positron emission tomography (PET)–CT revealed increased fluorodeoxyglucose uptake, with a maximum standardized uptake value of 8.3. Diffusion-weighted magnetic resonance imaging (MRI) revealed extreme hypointensity. He underwent total thymectomy by median sternotomy for presumed multiple thymoma. On histopathological analysis, cholesterol granuloma of the thymus was confirmed, and the patient had an uneventful postoperative course without recurrence for 28 months. Cholesterol granuloma of the thymus is a PET–CT-positive benign tumor with unique histological findings. The MRI findings were indicative of hypocellularity associated with a benign entity, whereas the PET–CT findings corresponded to granulomatous inflammation. Therefore, concurrent use of PET–CT and MRI can be helpful in distinguishing between benign cholesterol granulomas and malignant anterior mediastinal tumors.

Keywords: cholesterol granuloma, thymus, anterior mediastinum, positron emission tomography, magnetic resonance imaging

Introduction

Cholesterol granulomas are benign conditions characterized by cholesterol clefts and multinucleated giant cells that commonly develop in the middle ear and

paranasal sinuses.¹⁾ Cholesterol granuloma of the thymus is extremely rare, sometimes presenting as multifocal lesions in the anterior mediastinum.^{2,3)} Herein, we report a rare case of multifocal cholesterol granulomas of the thymus mimicking a thymic epithelial tumor.

Case Presentation

A 45-year-old man with an incidental finding of anterior mediastinal masses by routine computed tomography (CT) was referred for further investigation. His medical history included dyslipidemia and fatty liver disease. He had no history of trauma. Enhanced CT showed a 4.2-cm mass in the anterior mediastinum with slight contrast enhancement and spotty calcification, surrounded by 3 lesions measuring up to 0.8 cm (**Fig. 1A**). Contrast-enhanced magnetic resonance imaging (MRI) showed homogeneous hypointensity on both T1- and T2-weighted images without contrast enhancement (**Fig. 1B**). Diffusion-weighted

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Fig. 1 Preoperative imaging findings. (A) Coronal enhanced CT scan. Multiple lesions up to 4.2 cm in the anterior mediastinum had slight contrast enhancement and spotty calcification. (B) Contrast-enhanced MRI. A homogeneous mass in the anterior mediastinum without contrast enhancement was presented (arrow). (C) DWI. The signal intensity was extremely low (arrow). (D) PET-CT. A high FDG uptake with a maximum standardized uptake value of 8.3 was revealed. CT: computed tomography; MRI: magnetic resonance imaging; DWI: diffusion-weighted imaging; PET: positron emission tomography; FDG: fluorodeoxyglucose

imaging (DWI) revealed an image with extremely low signal intensity (**Fig. 1C**). Positron emission tomography (PET)-CT showed higher fluorodeoxyglucose (FDG) uptake in the main tumor with a maximum standardized uptake value of 8.3 (**Fig. 1D**). Total cholesterol (240 mg/dL) and triglyceride (340 mg/dL) levels were slightly elevated. Tumor markers, including carcinoembryonic antigen, alpha-fetoprotein, human chorionic gonadotropin, soluble IL-2 receptor, and anti-acetylcholine receptor antibody levels, were within normal ranges.

A highly aggressive thymic epithelial tumor was suspected from enhanced CT and PET-CT findings, and the patient consented to total thymectomy through a median sternotomy approach. Intraoperatively, there were firm and well-circumscribed masses in the left lobe of the thymus. The main tumor was $4.3 \times 3.0 \times 1.5$ cm in size with a dark red cut surface, and small-sized nodules up to 1.0 cm were also seen. Microscopically, these tumors contained numerous cholesterol clefts surrounded by multinucleated giant cells and histocytes, which formed granulomas (**Fig. 2A**). Focal hemorrhage, hemosiderin deposition, calcification,

and osseous metaplasia were also observed (**Fig. 2B**). There was no evidence of malignancy. Finally, a pathological diagnosis of cholesterol granuloma of the thymus was made. The patient's postoperative course was uneventful without recurrence for 28 months.

Discussion

Cholesterol granuloma is a benign mass containing cholesterol clefts and multinucleated giant cells that commonly develop in the middle ear and paranasal sinuses.¹⁾ Cholesterol granuloma of the thymus is extremely rare, whose exact pathogenesis remains unclear but is thought to involve focal microhemorrhages via angiopathy resulting from trauma, chronic inflammation, or dyslipidemia, as in our patient. The angiopathy induces deposition of cholesterol clefts that stimulate a foreign-body giant-cell reaction and granuloma formation.¹⁻⁶⁾

Cholesterol granulomas resemble thymic epithelial tumors on diagnostic imaging and can be difficult to detect preoperatively. We suspected a high-grade

Fig. 2 Pathological findings. **(A)** The low-power view. Numerous cholesterol clefts with surrounding multinucleated giant cells and histocytes, which comprised a granuloma (hematoxylin–eosin staining). **(B)** The high-power view. Cholesterol clefts with hemorrhage, hemosiderin deposition, calcification, and osseous metaplasia (hematoxylin–eosin staining).

multiple thymoma considering the multifocal mediastinal lesions, and high FDG uptake on CT and PET–CT images, which is usually observed in hypercellular tumors and malignancies. However, it is interesting to note that benign inflammatory masses such as cholesterol granuloma of the thymus also show remarkable FDG uptake because of granulomatous inflammation.^{3–5)}

MRI is used to distinguish benign from malignant mediastinal tumors.⁷⁾ The MRI features of cholesterol granulomas of the thymus have rarely been reported.⁵⁾ In the present case, extremely low signal intensity on both T1- and T2-weighted images reflected fiber, calcium, or hemosiderin. Cystic thymomas with chronic intratumoral hemorrhage can exhibit similar signals reflecting fibrosis, calcification, and hemosiderin.⁸⁾ Nevertheless, unlike our case, images with heterogeneous intensity are often seen in cystic thymomas. Furthermore, the lack of contrast enhancement and hypointensity on DWI indicated hypocellularity. Histologically, the tumor was composed of non-cellular components, such as cholesterol clefts (**Fig. 2A** and **2B**). This case demonstrates the value of MRI with the addition of PET–CT to differentiate cholesterol granulomas from malignant mediastinal tumors.

Multiple thymoma typically presents as multifocal anterior mediastinal tumors^{9,10)}; however, two cases of cholesterol granuloma of the thymus presenting as multifocal lesions have been reported.^{2,3)} Therefore, cholesterol granulomas should be considered in the differential diagnosis of multiple anterior mediastinal tumors.

There have been no reports on cholesterol granulomas of the thymus diagnosed preoperatively. A preoperative

biopsy is difficult for anatomical reasons,^{2,3)} and the presence of cholesterol clefts on histology is insufficient to confirm the diagnosis because cholesterol clefts can also be found in thymic cysts or thymomas.⁶⁾ As cholesterol granulomas do not recur after complete resection,^{2,3,5,6)} surgical resection and pathological evaluation are important for the proper diagnosis and treatment of this unique tumor.

Conclusion

Herein, we report a case of multifocal cholesterol granulomas of the thymus. Cholesterol granuloma is a PET-positive benign tumor of the thymus that mimics a thymic epithelial tumor. Concurrent use of PET–CT and MRI can be helpful in distinguishing benign cholesterol granulomas from malignant anterior mediastinal tumors.

Disclosure Statement

The authors have no conflicts of interest.

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